REMARKS/ARGUMENTS

I. Summary

Claims 1-13 are pending in the application. In the non-final Office Action mailed March 9, 2007 claims 1-13 have been rejected. Applicants note with appreciation the Examiner's withdrawal of the Election/Restriction requirement and consideration of claims 1-13.

The issues in the Office Action are:

- Claims 1-13 have been rejected under 35 U.S.C. § 112, first paragraph as not complying with the written description requirement;
- Claims 1-13 have been rejected under 35 U.S.C. § 112, first paragraph as not complying with the enablement requirement;
- Claims 1-13 have been rejected under 35 U.S.C. § 102(e) as being anticipated by *Hellberg et al.* (WO 03/027275, hereinafter *Hellberg*); and
- Claims 1-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatenable over claims 1-55 of copending U.S. Application No. 10/488,496.

Applicants respectfully traverse the Examiner's rejection of the claims for the reasons set forth below.

New claims 14 and 15 have been added to claim specific CTGF inhibitors and modulators recited in the specification. No new matter has been added.

II. Claim Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-13 have been rejected under 35 U.S.C. § 112, first paragraph as not complying with the written description requirement or the enablement requirement.

Written Description

Applicants note that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *See In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). *In re Wertheim* requires that the Examiner show, by a preponderance of evidence, that a person skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. Here, Applicants respectfully assert that the Examiner has not met the evidentiary showing required by *In re Wertheim*.

Applicants have disclosed in the specification assays to determine whether tested compounds modulate CTGF gene expression. *See* specification, Examples 1 and 2. Applicants have also disclosed specific class examples of CTGF inhibitors, including the GSK-3, CDK, and PPAR agonist classes. *See* specification, pages 10-11. In addition, Applicants have disclosed specific compounds that function as CTGF inhibitors. Certain of these compounds are presented with experimental data; for example, the compounds known as GW-8510 and SB-216763 are specifically discussed and presented with data. *See* specification, Figs. 3 and 4.

MPEP 2163.01 states that an Examiner, when rejecting a claim under 35 U.S.C. § 112, paragraph 1, set forth express findings of fact supporting the lack of written description conclusion. These findings should identify the claim limitation at issue. Here, the Examiner explains that the claimed "non-nucleotide or non-protein agent" limitation is at issue. Applicants again respectfully note that multiple classes and compounds that function as CTGF inhibitors are disclosed in the specification, and many of the specific classes and compounds are non-nucleotide or non-protein agents. Applicants also respectfully note that claim 1 is drawn to "at least one non-nucleotide or non-protein agent that inhibits expression, signaling or biological functions of CTGF". Applicants respectfully assert that they have provided in the specification descriptions of several agents that inhibit the expression, signaling or biological functions of CTGF. Accordingly, Applicant believe that the rejection of claims 1-13 under 35 U.S.C. § 112, paragraph 1 for insufficient written description is not proper and request that the Examiner withdraw this rejection.

Enablement

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *See* M.P.E.P § 2164.01, citing *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Furthermore, "[a] patent need not teach, and preferably omits, what is well known in the art." Id., citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991).

The Applicants have presented data showing that CTGF gene expression is elevated in glaucomatous trabecular meshwork ("TM") tissue when compared to normal TM tissue. *See* specification, Figs. 1 and 2. The Applicants further disclose CTGF's role in extracellular matrix ("ECM") production and its role in ECM production in the TM. *See* specification, pages 6 and 7. As discussed above in the remarks regarding the written description rejection, Applicants have disclosed assays needed to identify compounds with CTGF modulatory activity. Once compounds are identified as CTGF inhibitors using the disclosures of the present application, it is within the skill of one of ordinary skill in the art to test such compounds for intraocular pressure-lowering activity using *in vivo* models known at the time the application was filed. *See* e.g., Morrison et al., "Glaucoma Drops Control Intraocular Pressure and Protect Optic Nerves in a Rat Model of Glaucoma", IOVS, Vol. 39(3):526-531, March 1998 (copy attached hereto).

The Examiner states that it would require undue experimentation to (i) identify compounds with intraocular pressure-lowering activity and (ii) determine an effective amount of such compounds. As discussed above, assays are known that would allow one of skill in the art to identify compounds of the present invention with such activity. Furthermore, such assays would also allow one of skill to determine effective amounts of such compounds. Applicants have also identified a possible concentration range in a topical ocular formulation having a CTGF inhibitor present at a concentration of 0.005-5.0 wt. %. Applicants also note that the fact that experimentation may be complex does not necessarily make it undue experimentation, if the art typically engages in such experimentation. *See* M.P.E.P. § 2164.01, citing *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (*Intl. Trade Comm'n* 1983).

The Examiner further states that the specification does not teach one of skill in the art how to make and use the claimed invention. As long as the specification discloses at least

one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *See* M.P.E.P. § 2164.01(b). Applicants have disclosed specific CTGF inhibitors such as GW-8510 that can be used with embodiments of the present invention. Applicants have further provided a topical ocular formulation that can be used with such specific CTGF inhibitors. Accordingly, Applicants respectfully assert that the as-filed disclosure teaches one of skill in the art how to make and use the claimed invention.

In view of the above, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-13 under 35 U.S.C. § 112.

III. Claim Rejections under 35 U.S.C. § 102(e)

Claims 1-13 have been rejected under 35 U.S.C. § 102(e) as being anticipated by *Hellberg*. For a reference to be anticipatory, the identical invention must be shown in as complete detail as is contained in the claim. *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1566 (Fed. Cir. 1989). Also, the claim elements must be arranged as required by the claim. *See* M.P.E.P. § 2131 (citing *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The present inventors have recognized that agents that regulate, inhibit, or modulate the activity of connective tissue growth factor (CTGF) can lower intraocular pressure. While *Hellberg* teaches the use of GSK-3 inhibitors for lowering intraocular pressure, *Hellberg* does not recognize that the broader class of CTGF inhibitors can be used in this manner. The present inventors have provided disclosures showing that compound classes with CTGF modulatory activity, such as CDK inhibitors and PPAR agonists (in addition to GSK-3 inhibitors), may be useful to lower intraocular pressure, and have further disclosed techniques used to select and/or identify such compounds. *Hellberg* does not mention the broader use of CTGF inhibitors discovered by the present inventors, and accordingly does not show the identical invention in complete detail. Thus, *Hellberg* does not meet the standard set forth in *Richardson*.

In view of the above, Applicants respectfully assert that claims 1-13 are not anticipated by *Hellberg*, and request that the Examiner withdraw the rejection of record under 35 U.S.C. § 102(e).

IV. Double-patenting Claim Rejections

Claims 1-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatenable over claims 1-55 of copending U.S. Application No. 10/488,496. Under 37 C.F.R. § 1.130(c), obviousness-type double patenting rejections may be obviated by filing a terminal disclaimer in accordance with 37 C.F.R. § 1.321(c). Accordingly, Applicants propose filing a terminal disclaimer if the Examiner's rejection of these claims still stands upon Notice of Allowability of the present case.

V. Conclusions

For the reasons presented above, Applicants respectfully request that the Examiner withdraw the rejections of record and pass claims 1-15 to allowance. Applicants have included a petition under 37 C.F.R. §1.136 for a three (3) month extension of time and believe no further fees are due. However, if additional fees are due, please charge our Deposit Account No. 50-1051 in the name of Alcon, Inc.

Respectfully submitted,

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Date

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